REMARKS

The Applicant hereby submits the present *Amendment And Request For Reconsideration*, entry of which is earnestly requested. In an effort to reduce and resolve the issues, the Applicant amends claims 1-3, 12, 15-17, and 26. Thus, claims 1-29 which include independent claims 1 and 15 remain for reconsideration upon entry of the Amendment. No new matter has been added by this Amendment.

In the Office Action mailed on 3 November 2004, the Examiner rejected claims 1-3, 5-17, and 19-28 under 35 U.S.C. Sect. 112, first and second paragraphs. In response, the Applicant amends claims 1-3 and 15-17 to clarify. Support for these amendments may be found in the present application, for example, at pages 17-23 (e.g. see preferred primer selection rules on pp. 20-21 and 22-23).

With respect to claims 1 and 15, the term "prestored gene family data" has been modified to "gene family data of the gene sequence stored in a file." Although the Applicant disagrees with the Examiner's argument regarding the term "prestored," the language has been modified so as to provide further clarity to one skilled in the art. With respect to claims 2 and 16, the term "one or more ranges of acceptable lengths" has been modified to "one or more predetermined ranges of lengths." With respect to claims 3 and 17, the limitation "identified for two or more coding regions if they are sufficiently close together" has been modified to "identified for two coding regions if one coding region is within a predetermined number of nucleotide base identifiers from the other coding region." See e.g. page 21 at lines 3-15. Again, the language has been modified so as to provide further clarity to one skilled in the art. With respect to claims 12 and 26, the term "prestored" has been modified to "predetermined." Support for all of these amendments in general may be found in the present application at pages 17-23 (e.g. preferred primer selection rules on pp. 20-21 and 22-23). Based upon the above clarifications, the Applicant respectfully submits that the rejections under 35 USC Sect. 112 have been overcome.

In the same Office Action, the Examiner rejected claims 1 and 5-8 under 35 USC Sect. 102(b) as being anticipated by Hwang et al. citing a document entitled "Identification and characterization of a new member of the placental prolactin-like protein-C (PLP-C) subfamily, PLP-Cβ" (Endocrinology 2000 Sep;141(9):3343-52).

The standard for invalidity for anticipation from the prior art is well-established. "A prior art reference anticipates a patent claim if the reference discloses, either expressly or inherently, all of the limitations of the claim." EMI Group N. Am., Inc. v. Cypress Semiconductor Corp., 268 F.3d 1342, 1350 (Fed. Cir. 2001) (citations omitted). Applicant respectfully submits that the prior art described in the publication cited by the Examiner does not teach a method of processing gene sequence data comprising all the limitations of the pending claims. In particular, the following elements cannot be said to have been anticipated by the prior art in the cited publication.

For one, *Hwang et al. do not teach or suggest the step of identifying primer pair data following a set of primer selection rules which include "a first rule specifying that the primer pair data for the coding sequence be obtained for a predetermined annealing temperature" and repeating such identification for subsequent primer pair data.* The Examiner directs the Applicant's attention to p. 3346 at col. 2 and p. 3349 at the paragraph bridging cols. 1-2, which does not teach or suggest what is claimed.

Applicant submits that the last paragraph of the methods section of Hwang et al. describes a type of standard experimental protocol for expansion of cDNA using the polymerase chain reaction (PCR). Applicant also acknowledges that the PCR protocol which the authors followed specifies certain set temperatures for denaturation, for annealing, and for expression of the sample cDNA. The authors specify certain time duration intervals for the several serial reaction phases within each PCR round or cycle, and specify a certain number of cycles for the PCR protocol. In addition, the authors specified certain defined oligonucleotide sequences for their three constructed primer pairs.

Based on the above, however, it cannot be inferred that the authors had intended to specify their oligonucleotide sequences on the basis of any particular annealing temperature. To the contrary, their intention in specifying the sequences of their constructed primer pairs was clearly directed to other stated purposes, i.e., obtaining isoform-specific amplification. Thus, it should be clear that the selected primer pairs

were incorporated for use into a type of standard PCR protocol, in which experimental samples are subjected to certain temperatures for certain time intervals, regardless of the particular nucleotide sequence of the primers. The oligonucleotide sequences of the primer pairs were not specified or selected on the basis of any particular annealing temperature, nor on the basis of any other particular temperature. In fact, as shown in the results of Fig. 8, and as further discussed in the descriptive caption accompanying the same, the authors did not fully accomplish or demonstrate differential expression of the two isoforms. According to their explanatory hypothesis, the avidity of binding for the primers specific to the full-length isoform may have been substantially greater than the binding avidity for the primers specific to the deletion isoform.

Thus, the authors clearly did not intend to specify the sequence of their primer pairs with a particular purpose of providing a positive control to obtain maximal annealing at some predetermined temperature, or in conformance with some predetermined annealing temperature. In fact, as their results show, their two sets of primers demonstrated distinctly different degrees of annealing. That is, the two primers exhibited clearly different efficiencies of annealing during a series of PCR reactions wherein the annealing temperature was held constant and invariant, according to the standard methodology of the PCR protocol described. Thus, it cannot be said that the primers were chosen or selected for their having a similar, or even approximately similar, annealing behavior, at the annealing temperature of the PCR protocol described.

Since all claims require the step of identifying primer pair data following a set of primer selection rules which include "a first rule specifying that the primer pair data for the coding sequence be obtained for a predetermined annealing temperature," and repeating such identification for subsequent primer pair data, steps which are not found in the prior art, this rejection should be withdrawn.

Secondly, Hwang et al. do not teach or suggest the step of *identifying primer pair data following a set of primer selection rules which include "a second rule specifying that, based on a comparison of the primer pair data and gene family data of the gene sequence stored in a file, the primer pair data for the coding sequence must fail to match*

the gene family data" and repeating such identification for subsequent primer pair data. The Examiner directs the Applicant's attention to p. 3349 at the paragraph bridging cols. 1-2, and describes that Hwang et al "found a 3'-primer that did not match the gene family data of PLP-Cβ genes, which allowed him [sic] to only amplify one isoform," which does not teach or suggest what is claimed.

In Hwang et al., the two separate 3'-primers that were synthesized for purposes of PCR amplification were substantially similar, having an overlapping region comprising ten consecutive nucleotides. However, it should be evident that the strategy for selection of nucleotides in construction of the primer pairs was determined entirely by the sequence of the primer target regions, the nucleotide sequences proximate to the 5' and 3' opposite ends of the segment to be amplified. These sequences were not so much chosen as they were required, as a matter of necessity, for purposes of obtaining amplification using a type of standard experimental protocol that is well known in the art. It is of course true that the two pairs of primers were not identical; however, the reason for this fact is not attributable to an intentional introduction of dissimilarity. In fact, it might have been entirely possible that the 5' primer and one 3' primer might have shared identical similarity of sequence, had their hybridization target regions also been identical. While the two 3' primers were constructed to be dissimilar, this fact cannot be said to have resulted from any particular intention or concern of the authors to apply two distinctly different primers. Rather, their dissimilarity was entirely defined within the purpose of the PCR protocol, to obtain differential expression of the two slightly dissimilar isoforms. Furthermore, an experimental protocol designed to differentiate between two isoforms of the same protein is not conceptually equivalent with differentiating between different members of a gene family. According to the generally accepted and conventional definition, the meaning of the latter term implies a multiple grouping of two or more distinctly separate genes, derived either from distinctly separate chromosomal locations within one genome, or indeed from entirely distinct biological species.

Since all claims require the step of identifying primer pair data following a set of primer selection rules which include "a second rule specifying that, based on a comparison of the primer pair data and gene family data of the gene sequence stored in a file, the primer pair data for the coding sequence must fail to match the gene family data," and repeating such identification for subsequent primer pair data, steps which are not found in the prior art, this rejection should be withdrawn.

Thirdly, Hwang et al. do not teach or suggest the subsequent step of *"simultaneously amplifying the plurality of coding sequences in gene sequences from three or more individuals at the predetermined annealing temperature using the identified pairs of primer sequences, such that a plurality of amplified coding sequences from the three or more individuals are obtained."* The Examiner directs the Applicant's attention to p. 3346 at col. 2 and p. 3349 at the paragraph bridging cols. 1-2, which does not teach or suggest what is claimed. In this rejection, the Examiner specifically states that, in Hwang et al., "three or more strands of DNA ... is present after the initial PCR amplification of PLP-Cβ."

Regarding Hwang et al., the presumption of "three or more strands of DNA [being] present after the initial PCR amplification" is unfounded to the extent that only two strands might be present after the first PCR cycle, if only one strand of cDNA is present in the sample, to begin with. There is no proper presumption in any PCR amplification that even one double helix might in fact exist in the experimental sample. It is equally plausible to suppose that PCR might amplify one strand, separated away from one double-helical molecule of DNA, as to suppose that a given experimental sample might contain two, or three, or any other number of target strands. The entire purpose of the PCR methodology is to provide a suitable environment for such amplification to occur, using a reaction buffer containing sufficient primers and enzyme, and a sufficient supply of monomer nucleotides, such as to facilitate expansion of even the slightest trace of the target DNA.

Further, it cannot be said that the cited publication provides an example of where PCR amplification was simultaneously conducted on samples of DNA obtained from

three or more individuals. The amplified cDNA may have been from derived from one individual, one experimental animal, per each amplification. Similarly, amplification of cDNA obtained from mRNA samples harvested from tissue may very likely have involved a particular sample of mRNA from one experimental animal, or indeed might have been derived from one tissue slice, per each amplification.

Since all claims require the step of "simultaneously amplifying the plurality of coding sequences in gene sequences from three or more individuals at the predetermined annealing temperature using the identified pairs of primer sequences, such that a plurality of amplified coding sequences from the three or more individuals are obtained," which is not found in the prior art, this rejection should be withdrawn.

In the same Office Action, the Examiner also rejected claims 15, 19, and 20-22 under 35 USC Sect. 103(a) as being unpatentable over Hwang et al. Although the Applicant disagrees with the Examiner's rejections with respect to these claims, such rejections are moot in light of Applicant's arguments presented above.

The Applicant respectfully requests entry of this Amendment And Request For Reconsideration. Since the amended claims 1-29 are allowable over the prior art of record, and no issues under Sect. 112 remain, the application is now in a condition suitable for allowance.

Thank you for your reconsideration. Please feel free to contact the undersigned for any reason if it would expedite the prosecution of the present application.

Respectfully Submitted,

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